REMARKS

In this Amendment, Applicant has cancelled Claims 27 – 40 and 42 – 44 without prejudice or disclaimer, amended Claims 1 – 26 and added new Claim 45. Claims 1 – 26 have been amended to specify various embodiments of the present invention and overcome the rejection. In addition, the specification has been amended to rephrase certain expressions and correct clerical errors. The amendment is editorial in nature. It is respectfully submitted that no new matter has been introduced by the amended claims and specification. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

INFORMATION DISCLOSURE STATEMENT:

The Examiner indicated that certain reference listed in the PTO 1449 form of the Information Disclosure Statement (IDS) filed on August 5, 2003 could not be found. Applicant respectfully submits the reference AD was previously filed on August 5, 2003. Enclosed please find the copies of the IDS, PTO-1449 and stamped postcard showing all 13 references were submitted. In any event, Applicant hereby respectfully provides the copy of the missing reference (AD) indicated by the Examiner for consideration.

OBJECTION TO SPECIFICATION:

The specification has been objected as containing informality.

It is respectfully submitted that the informalities contained in the specification have been corrected as follows:

In page 4, line 24, "SEQ. ID. NO. 1" has been changed to "SEQ ID NO: 1." The same change has been made throughout the specification.

In page 4, line 35, "SEQ ID NO: 4" has been inserted after "KKLVFFA"; please note that this sequence is different from the sequence identified as SEQ ID NO: 3. A new sequence

listing in both paper form and computer readable form has been hereby submitted to include the SEQ ID NO: 4;

In page 9, line 30, it is respectfully submitted that, in the specification, "R" groups have not been included in the formula of the proposed peptide back-bone replacement groups, because these peptide back-bone replacement groups would not then be able to replace the CONH groups within the peptide backbone. For example, the nitrogen atom in CONH forms three bonds (two with the neighboring carbon atoms in the peptide backbone and one with the hydrogen atom), but the oxygen atom in COO only forms two bonds (one with each of the neighboring carbon atoms in the peptide backbone). Therefore, COOR would be incorrect, because such a group would not be able to replace the CONH group by forming a bond with each of the two neighboring carbon atoms in the peptide backbone. In addition, "(thioester)" has been added after "COS" and "(dithioester)" has been added after CSS, according to Examiner's suggestion.

In page 17, line 6, "monomers are amino-acids" is changes to "amino acid residues" according to Examiner's suggestion. The same change has been made throughout the specification.

In addition, "α-L-amino-acids" is changed to "α-L-amino acid" throughout the specification.

Therefore, objection to the specification is overcome and withdrawal of the objection is respectfully requested.

OBJECTION TO CLAIMS:

Claims 1, 7, 15, 16, 21, 23, 24 and 26 have been objected as containing informality.

It is respectfully submitted that the objection has been overcome by the presently submitted amendments.

In Claim 1, "α-L-amino-acids" is changed to "α-L-amino acid." The same change has been made in the applicable dependent claims.

In Claim 7, it is respectfully submitted that the term "β-sheet propensity" should NOT be changed to "β-structure propensity", because "β-sheet propensity" is the technical term that is used in many biochemistry textbooks and is more familiar to those skilled in the art. In addition, "β-sheet propensity" is clearly defined on page 18 of the specification and at no stage does Applicant use the term "β-structure propensity".

In Claims 15 – 16, "SEQ ID NO: 5" has been added after the amino acid sequence KLVFFAE.

In Claim 21, the term "inclusion" does not exist. Therefore, the objection is incorrect.

In Claims 23 – 24, "SEQ. ID. NO. " has been amended to "SEQ ID NO:".

In addition, Claim 26 has been amended the same way as the changes on page 9, line 30 of relevant part of the specification.

Therefore, objection to Claims 1, 7, 15, 16, 21, 23, 24 and 26 are overcome and withdrawal of the objection is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112 SECOND PARAPGRAPH:

Claims 1 – 26 and 41 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is respectfully submitted that the rejections have been overcome by the presently submitted amendments.

Claim 1 has been amended to clearly define the embodiments of the present invention. In the amended Claim 1, the term "Nα-substituted" has been amended to specify that "the Nα-atoms within the peptide backbone of the β-strand is Nα-substituted with an Nα-substituent." In addition, "a separate peptide-containing molecule" has not been amended, because it clearly refers to "a separate molecule that contains a peptide."

Furthermore, Claim 1 has been substantially amended to clarify its intended scope by introducing the following amendments:

- the length of the β-strand-forming section of peptide has been limited to between four and sixteen consecutive α-D-amino acid residues. The support can be found on page 17, lines 12 – 13 of the specification;

- the β-strand-forming section of peptide has been defined as being at least 50% of said peptide. The support can be found on page 8, lines 34 – 35 of the specification;

- the peptide backbone has been further defined as taking the form of an extended ribbon. The support can be found on page 7, lines 24 – 29 of the specification;

- the term "edges" has been further defined by reference to the NH and CO components of the backbone peptide groups which lie along the two edges of the ribbon, not the terminals as interpreted by the Examiner. The support can be found on page 7, lines 24 – 29 of the specification; and

- the reference to "any two successive Nα-substituted α-D-amino acid residues [being] separated by an odd number of consecutive Nα-substituted α-D-amino acid residues" has been added to new Claim 45 which depends on Claim 1.

In Claim 2, the term "Nα-unsubstituted amino-acid residues" has been amended to clearly refers to "Nα-unsubstituted α-D-amino acid residues."

Claim 3 has been amended to introduce the term "the" before "successive Nα-substituted α-D-amino acid residues." The typographical error has been corrected by adding a hyphen "-" between "Nα" and "substituted α-D-amino acid residues" in Claim 1. Therefore, there is antecedent basis for this term in Claim 1.

Claim 4 has been amended such that the Nα-substituent hinders association of the second edge of the β-strand with any other β-strand, whether this other β-strand forms part of a separate peptide-containing molecule or part of the same molecule. This clarifies that the said association may be either intermolecular *or* intramolecular. The fact that the Nα-substituent is sterically hindering association of the said second edge makes it irrelevant whether it is hindering intermolecular or intramolecular association. It is simply inhibiting any association of the second edge with another β-strand. In addition, the antecedent basis for "the Nα-substituent" has been provided in Claim 1.

Regarding Claim 6, the amendment to Claim 1 provides antecedent basis for the term "the side chain".

Claim 8 has been amended to introduce a hyphen between "β-strand" and "forming".

Claim 10 has been amended to delete "the" indicated by the Examiner. Regarding the term "stacking of β-sheets", it is respectively submits that this term is clear and definite as the prevention of β-sheet stacking is discussed in detail on page 29 of the specification. A person of ordinary skill in the art can easily understand the meaning of this term.

Regarding Claim 11, it is respectfully submitted that the term "extends beyond" is clearly defined on page 29, lines 20-30 of the specification of the present application as filed. This term is clear to a person skilled in the relevant art, who is aware of the problem of β-sheets stacking.

Regarding Claim 12, the amendment to Claim 1 to refer to "a side chain able to form favourable non-covalent interactions" provides antecedent basis for the phrase "the side chain" in Claim 12. In addition, Claim 12 has been amended to indicate that "the side chain of one or more α-D-amino acid residues in the β-strand-forming section of peptide contains a detectable group which allows the compound or composition to be traced or detected." The support can be found on page 30, lines 3 – 21 of the specification.

In Claim 14, "glycine" has been deleted following the Examiner's suggestion. The amendment to Claim 1 to refer to "a side chain able to form favourable non-covalent interactions" provides antecedent basis for the phrase "the side chain" in Claim 14.

Regarding Claim 17, the phrase "biological barriers such as cell membranes and the blood-brain barrier" has been amended to "cell membranes, the blood-brain barrier or any other biological barrier". The antecedent basis for the term "the side chain" has been provided in Claim 1. In addition, "or" has been added between "preceded by" and "followed by" according to Examiner's suggestion.

In Claim 19, the term "or" has been added between "free" and "amidated" according to Examiner's suggestion.

In Claim 20, "the" has been added before the "peptide" according to Examiner's suggestion. Applicant respectively submits that the term "attached" is clearly defined on page 33, line 22 through page 34, line 9 of the specification where a number of attachment means are proposed, together with how attachment of the functional group may be performed. A person of ordinary skill in the art can easily understand the meaning of this term.

Claim 22 has been amended to rephrase various expressions which is sufficient to overcome the rejection.

Claim 23 has been amended to specify that "a sequence of said chains" is a part of "amino acid residues of the β-strand forming section of the peptide. In addition, it is respectfully submits that, based on the general teaching of the application, it would be clear to the skilled person in the art that the term "homologous to" is intended to mean, primarily that it is functionally similar to SEQ ID NO: 3, but that does not prevent it from also being structurally similar to SEQ ID NO: 3. This claim is dependent on Claim 1, so the β-strand forming section of the peptide in Claim 23 must have the same functional and structural characteristics defined in Claim 1.

In Claim 25, the term "or instead of" has been deleted. The term "backbone peptide groups" is clearly described on page 9 line 21 through page 10 line 5 of the specification, and would be clear to a person skilled in the art as meaning CONH, if the backbone peptide is not Nα-substituted, or CON(R), if the H-atom of the backbone peptide group is Nα-substituted. In addition, the claim has been amended to clarify "the side-chain group" is part of the "amino acid residues of the β-strand-forming section of the peptide."

Claim 26 has been amended to clarify the alternative peptide backbone substitutions as described on page 9, line 21 through page 10, line 5 of the present application. It is respectively submitted that the phrase "the backbone peptide groups ... replaced by ..." refers to the CONH (Nα-unsubstituted) backbone peptide groups or CON(R), if the H-atom of the backbone peptide group is Nα-substituted. Taking into account the specific reference to either CONH or CON(R) as backbone peptide groups, and the structure of the replacement groups referred to in Claim 26, it is clear to a person of skilled in the art that "backbone groups" refers to both the backbone N-H (or N-(R)) and the backbone C=O forming a single unit. Part (c) of the amended Claim 26 clearly relates to replacement of the "side-chains" of the β-strand-forming section of peptide.

Therefore, the rejection under 35 U.S.C. § 112, second paragraph, has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 102:

Claims 1, 4 – 26 and 41 have been rejected under 35 U.S.C. § 102 (e) as allegedly being anticipated by Findeis, M.A. et al. (US Patent 6,610,658), hereinafter Findeis.

Applicant traverses the rejection and respectfully submits that the present-claimed invention is not anticipated by the cited reference. As indicated above, the amended Claim 1 further clarifies the scope of the embodiments of the present invention. More specifically, the amended Claim 1 defines "[A] 1.(currently amended) A chemical compound or composition comprising a peptide, wherein (a) said peptide comprises a β-strand-forming section of peptide consisting of four to sixteen consecutive α-D-amino-acid residues and encompassing at least 50% of said peptide;

(b) each of the consecutive α-D-amino acid residues in said β-strand-forming section of peptide has a side chain;

(c) said β-strand-forming section of peptide forms a β-strand having a peptide backbone which takes on the form of an extended ribbon having two edges, a first edge and a second edge, such that the NH and CO components of successive α-D-amino acid residues lie along the alternate edges of the ribbon;

(d) at least one of the Nα-atoms within the peptide backbone of the β-strand is Nα-substituted with an Nα-substituent, such that one or more Nα-substituent lie along only the second edge and sterically hinders the association of the second edge with another β-strand; and

(e) the first edge remains free of Nα-substituents, and is not prevented from associating with a target -strand formed by a separate peptide-containing molecule."

Claims 4 – 26 and 41 also include these features due to their dependency on Claim 1.

Especially, Claim 1 clearly defined that "said β-strand-forming section of peptide forms a β-strand having a peptide backbone which takes on the form of an extended ribbon having two edges, a first edge and a second edge, such that the NH and CO components of successive α-D-amino acid residues lie along the alternate edges of the ribbon." Therefore, it is clear that the "edge" is not N- or C-terminal region of compounds disclosed in Findeis as alleged. Applicant respectfully submits that it is incorrect to refer to the N-terminal region (Y-Xaa1-Xaa2) and the C-terminal region (Z-Xaa1'-Xaa2'-Xaa3'-) of the peptide disclosed in Findeis as being equivalent to the first edge and second edge as defined in of the amended Claim 1. The edges of

the extended ribbon formed by the backbone of the β-strand are not the terminals of peptide, as a person of ordinary skills in the art understands that the primary structure of a peptide is different from the secondary structure formed by a β-strand.

Findeis relates to modified β-amyloid modulators. It differs from the compounds of the present invention in that it modifies the compounds at (a) N-or C-termini, and/or (b) at the side chains of the peptide structure (col. 5, lines 43 – 45 and col. 14, lines 35 – 49). There is no discussion of modifying the Nα-substiuents in the peptide backbone of the β-strand such that the substituents lie along only one "edge" of the β-strand. A substitution at the N-termus would not fall within the scope of the amended Claim 1 because:
(a) it is not a substitution "within the peptide backbone of the β-strand"; and
(b) it would not "lie along only the second edge" because the C-N bond attaching the terminal NH2 group to the peptide can rotate. It is not a fixed conformation like the peptide backbone N-H components. The embodiment of the present invention as defined in the amended Claim 1 indicates that the H-atoms on Nα-atoms within the peptide backbone are substituted (See part (d) of Claim 1). Only the Nα-substitution fixes the conformation of the substituents and ensures that they align along a single edge of the peptide backbone of the β-strand.

In addition, regarding the Nα-subsitution, the Examiner refers to Example 11 of Findeis. However, there is no Example 11 in Findeis. The Examiner also states that the Nα modification referred to in col. 20, lines 47 – 60 is modification of a backbone Nα. However, this disclosure relates to modification of backbone Nα groups in "modifying groups", which is defined in col. 18. lines 26 – 28 of Findeis as a group "not naturally coupled to natural Aβ peptides in their native form." This is not a modification of Nα groups of the peptide backbone of the β-strand as in the amended Claim 1. Applicant respectfully submits that there is no disclosure in Findeis to modify the Nα-substituents in the peptide backbone of the β-strand and there is no teaching to suggest that the Nα-substituents could be positioned along one edge of the backbone.

Therefore, the newly presented claim is not anticipated by Findeis and the rejection under 35 U.S.C. § 102 (b) has been overcome. Accordingly, withdrawal of the rejection under 35 U.S.C. § 102 (b) is respectfully requested.

THE DISCLOSURE IN QUIBELL AND REJECTIONS UNDER 35 U.S.C. § 103:

The Examiner stated in page 2 of the office action that because Findeis make it obvious to replace L-amino acids with D-amino acids, the present invention is obvious over Quibell. This is based on the assumption that the use of D-amino acids is the only difference between the present invention and the compounds disclosed in Quibell. However, this assumption is incorrect.

The amended claims limit the length of the peptides of the present invention and distinguish it from the compounds in Quibell. More importantly, Quibell does not teach that "substitution of at least one of the Nα-atoms within the peptide backbone of the β-strand" is sufficient to hinder sterically one edge of a β-strand associating with another β-strand, whilst still allowing the other unsubstituted edge to "associate with a target β-strand formed by a separate peptide-containing molecule." Furthermore, Quibell fails to teach the positioning of additional Nα-substituents such that they "lie along only the second edge." These features of the embodiments of the present invention relates to compact β-amyloid inhibitors small enough to penetrate the blood barrier without compromising their potency.

Quibell discloses methods of synthesizing β-amyloids using large bulky blocking groups to prevent aggregation of a synthesized β-amyloid molecule with any other β-amyloid molecules in solution. The compounds disclosed in Quibell are never intended to associate with a separate peptide containing molecule. Therefore, Quibell teaches away from an important feature of the embodiment of the present invention which is to allow the association of one substituted edge of the β-strand with another separate peptide containing molecule, whilst blocking any association at the other substituted edge. This feature allows using substituted and unsubstituted edges in a single molecule to both associate, and block association, with separate peptide containing molecules.

Like the Quibell reference, Findeis fails to recognize the novel feature of the present invention. There is no reference in Findeis of using Nα-substituents within the peptide backbone to prevent association with a separate molecule along one edge of the molecule whilst allowing association along the second unsubstituted edge.

It is respectfully submitted that there is no teacing in either of these references which would lead the skilled person to look for a compound to inhibit β-amyloid aggregation, to palce one or more, Nα-substituents onto the peptide backbone of a β-strand such that they lie along only one edge of the peptide backbone, thus preventing association at the substituted edge but allowing it at the unsubstituted edge.

Therefore, the rejection under 35 U.S.C. §103 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. §103 is respectfully requested.

REQUEST FOR INTERVIEW:

Applicant respectfully requests a personal or telephone interview, if the Examiner believes that the present amendment will not put the application in condition for allowance. If an interview is granted, please contact the undersigned attorney at your earliest convenience.

Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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